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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
HOLLERAN, ANNE L	
ART UNIT	PAPER NUMBER
1643	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	03/08/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/619,754	BOSSENMAIER ET AL.	
	Examiner	Art Unit	
	Anne L. Holleran	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 December 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *23-28,40-52 and 64-73* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *23-28, 40-52, 64-73* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. The amendment filed 12/21/2006 is acknowledged. Claims 1-22, 29-39, 53-63 and 74-88 were canceled. Claims 23-28, 40-52 and 64-73 are pending and examined on the merits.

Claim Rejections Maintained and New Grounds of Rejection:

Claim Rejections - 35 USC § 112

2. Claims 23-28, 40-52, and 64-73 remain rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The amendment to claims 23, 47 and 71 fails to obviate the rejection under 35 U.S.C 112, second paragraph, because the amendment introduces further indefiniteness.

Claims 23, 47 and 71 are indefinite because it is not clear what is "a significant level of phophorylation".

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

3. Claims 23-28, 40, 42, 46-52, 64, 66, and 70 remain rejected under 35 U.S.C. 102(b) as being anticipated by Thor (Thor, A.D. et al., Journal of Clinical Oncology, 18(18): 2000, 3230-3239, 2000) for the reasons of record.

Applicants argue that the claim amendments to independent claims 23 and 47 add an affirmative step of identifying the tested Her2-positive tumor cells as responsive to treatment (claim 23) or predicting that a subject diagnosed with a Her2 positive tumor is likely to respond to treatment (claim 47), where in each case the treatment is an antibody inhibiting the association of Her2 with another member of the ErbB receptor family if the level of phosphorylation of an ErbB receptor in a biological sample obtained from the subject is at a significant level. Applicants also point out that original claim 71, containing an affirmative step of determining that a subject is likely to respond to treatment, was left out of this rejection in the previous Office action. However, claim 71 was not included in this rejection because the first active step of claim 71 requires a sample of circulating tumor cells, which is not taught by Thor. After careful consideration, the steps of either "identifying said Her2 –positive cells as responsive to treatment" or "predicting that said subject is likely to respond to treatment" are not considered to be active steps. Instead these phrases are considered to be recitations of mental activity. In a method claim, the presence of steps directed to mental activity does not serve to distinguish that claimed method over a prior art method containing active steps identical to active steps in the claimed method. Therefore, the rejection of record is maintained.

The following is a reiteration of the rejection in the previous Office action:

The claimed methods comprise the active steps of providing a biological sample comprising HER2-postive tumor cells and detecting the phosphorylation of an ErbB receptor in said biological sample. The phosphorylation of an ErbB2(HER2) receptor is detected. The sample may be tissue sample obtained from a tumor biopsy, and the tumor may be a breast tumor, and the ErbB receptor phosphorylation may be determined by immunohistochemistry. The intended use of the claimed methods is for identifying tumor cells as responsive to treatment with an antibody inhibiting the association of HER2 with another member of the ErbB receptor family, wherein the antibody binds HER2, or the anti-Her2 antibody blocks ligand activation of an ErbB heterodimer comprising HER2 or wherein the antibody is rhuMAb 2C4. The intended use may also be for predicting the response of a subject diagnosed with a HER2-positive tumor to treatment with an antibody inhibiting the association of HER2 with another member of the ErbB receptor family.

Thor teaches the use of immunohistochemistry to detect phosphorylation of ErbB2 in breast cancer tissue samples (see page 3232, 1st column and page 3233, 2nd column, description of Groups A, B and C, where groups B and C are patient groups that are ErbB2 positive and the phosphorylation of ErbB2 is detected). Thus, Thor teaches the claimed methods because Thor's methods comprise the same active steps as recited in the claims.

Thor's method does not appear to have the same intended use as the intended use set forth in the claims. However, the active steps in Thor are the same as in the claims and the intended use recited in the claims does not appear to materially affect the active steps of the claimed methods.

4. Claims 23-28, 40, 42-44, 47-52, 64, and 66-68 are rejected under 35 U.S.C. 102(b) as being anticipated by Wildenhain (Wildenhain, Y. et al., Oncogene, 5(6): 879-883, 1990; abstract only).

Applicants argue that the claim amendments to independent claims 23 and 47 add an affirmative step of identifying the tested Her2-positive tumor cells as responsive to treatment (claim 23) or predicting that a subject diagnosed with a Her2 positive tumor is likely to respond to treatment (claim 47), where in each case the treatment is an antibody inhibiting the association of Her2 with another member of the ErbB receptor family if the level of phosphorylation of an ErbB receptor in a biological sample obtained from the subject is at a significant level. Applicants also point out that original claim 71, containing an affirmative step of determining that a subject is likely to respond to treatment, was left out of this rejection in the previous Office action. However, claim 71 was not included in this rejection because the first active step of claim 71 requires a sample of circulating tumor cells, which is not taught by Thor. After careful consideration, the steps of either "identifying said Her2 –positive cells as responsive to treatment" or "predicting that said subject is likely to respond to treatment" are not considered to be active steps. Instead these phrases are considered to be recitations of mental activity. In a method claim, the presence of steps directed to mental activity does not serve to distinguish that claimed method over a prior art method containing active steps identical to active steps in the claimed method. Therefore, the rejection of record is maintained.

The following is a reiteration of the rejection in the previous Office action:

The claimed methods comprise the active steps of providing a biological sample comprising HER2-postive tumor cells and detecting the phosphorylation of an ErbB receptor in said biological sample. The phosphorylation of an ErbB2(HER2) receptor is detected. The sample may be tissue sample obtained from a tumor biopsy, and the tumor may be a breast tumor, and the ErbB receptor phosphorylation may be determined by immunopreciptiation of the ErbB receptor and Western blot analysis, where the ErbB receptor is indicated by the presence of a phosphor-ErbB receptor band on the gel. The intended use of the claimed methods is for identifying tumor cells as responsive to treatment with an antibody inhibiting the association of HER2 with another member of the ErbB receptor family, wherein the antibody binds HER2, or the anti-Her2 antibody blocks ligand activation of an ErbB heterodimer comprising HER2 or wherein the antibody is rhuMAb 2C4. The intended use may also be for predicting the response of a subject diagnosed with a HER2-positive tumor to treatment with an antibody inhibiting the association of HER2 with another member of the ErbB receptor family.

Wildenhain teaches the use of immunoblotting with anti-neu (anti-Her2 or anti-ErbB2) antibodies and antiphosphotyrosine antibodies to detect phosphorylation of ErbB2 in breast cancer tissue samples (see abstract). Thus, Wildenhain teaches the claimed methods because Wildenhain's methods comprise the same active steps as recited in the claims.

Wildenhain's method does not appear to have the same intended use as the intended use set forth in the claims. However, the active steps in Wildenhain are the same as in the claims and the intended use recited in the claims does not appear to materially affect the active steps of the claimed methods.

5. Claims 23-28, and 42-44 are rejected under 35 U.S.C. 102(b) as being anticipated by Xu (Xu, F.J. et al. Int. J. Cancer, 59: 242-247, 1994).

Applicants argue that the claim amendments to independent claim 23 add an affirmative step of identifying the tested Her2-positive tumor cells as responsive to treatment, where the treatment is an antibody inhibiting the association of Her2 with another member of the ErbB receptor family if the level of phosphorylation of an ErbB receptor in a biological sample is at a significant level. Applicants also point out that original claim 71, containing an affirmative step of determining that a subject is likely to respond to treatment, was left out of this rejection in the previous Office action. However, claim 71 was not included in this rejection because the first active step of claim 71 requires a sample of circulating tumor cells, which is not taught by Thor. After careful consideration, the step of "identifying said Her2 –positive cells as responsive to treatment" is not considered to be an active step. Instead this phrase is considered to be a recitation of mental activity. In a method claim, the presence of steps directed to mental activity does not serve to distinguish that claimed method over a prior art method containing active steps identical to active steps in the claimed method. Therefore, the rejection of record is maintained.

The following is a reiteration of the rejection in the previous Office action:

Xu teaches Western transfer to detect p185 (Her2) phosphorylation in SKBr3 breast cancer cells (see page 244: Figure 2, 1st column, first full paragraph, also Table I, and also page 244, 2nd column, 2nd paragraph). Therefore, Xu teaches the claimed methods because Xu's method comprises the same active steps as recited in the claims.

Xu's method does not appear to have the same intended use as the intended use set forth in the claims. However, the active steps in Xu are the same as in the claims and the intended use recited in the claims does not appear to materially affect the active steps of the claimed methods.

6. Claims 23-28, and 42-44 are rejected under 35 U.S.C. 102(b) as being anticipated by Ignatoski (Ignatoski, K.M.W., et al., Endocrinology, 140: 3615-3622, 1999).

Applicants argue that the claim amendments to independent claim 23 add an affirmative step of identifying the tested Her2-positive tumor cells as responsive to treatment, where the treatment is an antibody inhibiting the association of Her2 with another member of the ErbB receptor family if the level of phosphorylation of an ErbB receptor in a biological sample is at a significant level. Applicants also point out that original claim 71, containing an affirmative step of determining that a subject is likely to respond to treatment, was left out of this rejection in the previous Office action. However, claim 71 was not included in this rejection because the first active step of claim 71 requires a sample of circulating tumor cells, which is not taught by Thor. After careful consideration, the step of "identifying said Her2 –positive cells as responsive to treatment" is not considered to be an active step. Instead this phrase is considered to be arecitation of mental activity. In a method claim, the presence of steps directed to mental activity does not serve to distinguish that claimed method over a prior art method containing active steps identical to active steps in the claimed method. Therefore, the rejection of record is maintained.

The following is a reiteration of the rejection in the previous Office action:

Ignatoski teaches phosphotyrosine Western blot analysis of protein obtained from MCF-10erbB02 and H16N2erbB02 cells to detect $p185^{erbB2}$ phosphorylation (see page 3619: Figure 3, 1st column) and also to detect erbB-3 phosphorylation (page 3619, 2nd column) in MCF-10A and H16N2 breast cancer cells. Therefore, Ignatoski teaches the claimed methods because Igantoski's method comprises the same active steps as recited in the claims.

Igantoski's method does not appear to have the same intended use as the intended use set forth in the claims. However, the active steps in Igantoski are the same as in the claims and the intended use recited in the claims does not appear to materially affect the active steps of the claimed methods.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

7. Claims 23, 41, 47, 65 and 71-73 remain rejected under 35 U.S.C. 103(a) as being unpatentable over DiGiovanna (DiGiovanna, M.P. et al. Cancer Research 55: 1946-1955, 1995) in view of Terstappen (US 6,365,362; issued Apr. 2, 2002; effective filing date Nov. 30, 1998).

Applicants' arguments have been carefully considered, but fail to persuade. Applicants appear to be arguing that DiGiovanna fails to provide the requisite teachings to suggest using the steps of determining levels of phosphorylation of Her2 as a method to determine whether a patient is likely to respond to an anti-Her2 antibody. Applicants cite the low number of samples tested by DiGiovanna (5 samples). Applicants' arguments fail to persuade. DiGiovanna teaches that the extent of p185 (Her2) tyrosine phosphorylation varies considerably, and that it is highly likely that measurement of p185 signaling activity as opposed to p185 abundance will greatly enhance methods that use detection of p185 for prognosis and treatment decisions, and that tumors most vulnerable to anti-p185 antibodies will be those that are dependent upon p185 signaling for growth (see page 1954, 1st column; and also see abstract and also Introduction, page 1946, 2nd column). DiGiovanna then goes on to demonstrate use of one particular antibody, the

PN2A antibody. The fact that DiGiovanna does not have data from a large number of samples is not relevant to the conclusion that it would have been obvious to use DiGiovanna's method in a sample of circulating tumor cells, especially in light of the suggestion by DiGiovanna that measurement of P185 phosphorylation may be more clinically relevant than measurement of P185 abundance, and further in light of the teachings of Terstappen that methods of assaying circulating tumor cells immunocytochemically may be used to monitor patients for recurrence of cancer or for response to therapy, and teaches that levels of tumor markers such as Her2 may be assessed (see abstract; and column 8, lines 29-57 and column 9, line 54 – column 10, line 51). Therefore, the combination of the references suggests the claimed methods, which are interpreted as methods drawn to determining levels of phosphorylation of ErbB receptors in samples of circulating tumor cells. The steps added by amendment of either "identifying said Her2 – positive cells as responsive to treatment" or "predicting that said subject is likely to respond to treatment", or present in original claim 71 of "determining that said subject is likely to respond to treatment with an anti-Her2 antibody" are not considered to be active steps. Instead these phrases are considered to be recitations of mental activity. In a method claim, the presence of steps directed to mental activity does not serve to distinguish that claimed method over a prior art method containing active steps identical to active steps in the claimed method.

The original rejection is reiterated below:

Claims 71-73 are drawn to methods for identify a subject responsive to treatment with an anti-Her2 antibody, comprising detecting phosphorylation of an ErbB receptor in circulating

tumor cells and determining that the subject is likely to respond to treatment with an anti-Her2 antibody if phosphorylation is detected.

Claims 23, 41, 47 and 65 comprise methods where phosphorylation of an ErbB receptor in circulating tumor cells is detected.

DiGiovanna teaches use of immunohistochemistry on formalin-fixed and paraffin-embedded surgical specimens from human breast tumors (see page 1948, 1st column, and 1950, 1st and 2nd column, bridging paragraph) using the PN2A antibody, which is specific for phosphorylated Her2. DiGiovanna also teaches that the extent of p185 (Her2) tyrosine phosphorylation varies considerably, and that it is highly likely that measurement of p185 signaling activity as opposed to p185 abundance will greatly enhance methods that use detection of p185 for prognosis and treatment decisions, and that tumors most vulnerable to anti-p185 antibodies will be those that are dependent upon p185 signaling for growth (see page 1954, 1st column). DiGiovanna fails to teach the method using samples of circulating tumor cells.

However, Terstappen teaches that carcinoma cells in the blood may be assay immunocytochemically to characterize the circulating tumor cells. Terstappen teaches that the methods may be used to monitor patients for recurrence of cancer or for response to therapy, and teaches that levels of tumor markers such as Her2 may be assessed (see abstract; and column 8, lines 29-57 and column 9, line 54 – column 10, line 51).

Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have modified DiGiovanna's method so that it could be used in the measurement of Her2 phosphorylation status of circulating tumor cells. One would have been motivated to have combined the teachings of DiGiovanna and Terstappen because

collecting a blood sample to analyze the Her-2 status of circulating cancer cells is less invasive than collecting a tissue sample from the cancer.

8. Claims 23, 43, 45, 47, 67 and 69 remain rejected under 35 U.S.C. 103(a) as being unpatentable over DiGiovanna (DiGiovanna, M.P. et al. Cancer Research 55: 1946-1955, 1995) for the reasons of record.

Applicants' arguments are based on the arguments presented for the previous rejection under 103(a), and applicants repeat the assertion that DiGiovanna's method does not teach or suggest a method of determining the likelihood of responding to treatment with an anti-Her2 antibody. However, this argument is not found persuasive because it is not the intended use of a claimed method that is compared with the prior art, but instead the active steps of the claimed method. Tthe steps added by amendment of either "identifying said Her2 –positive cells as responsive to treatment" or "predicting that said subject is likely to respond to treatment", or present in original claim 71 of "determining that said subject is likely to respond to treatment with an anti-Her2 antibody" are not considered to be active steps. Instead these phrases are considered to be recitations of mental activity. In a method claim, the presence of steps directed to mental activity does not serve to distinguish that claimed method over a prior art method containing active steps identical to active steps in the claimed method. Therefore, the rejection of record is maintained. The previous rejection is reiterated below:

The claimed methods encompass methods of detection of Her2 phosphorylation comprising first using immunoblot techniques to detect phosphorylated Her2 and then

confirming the result with immunohistochemistry using a phospho-specific anti-ErbB2 receptor antibody.

DiGiovanna demonstrates an immunoblot technique, where a phosphor-ErbB receptor band on a gel is detected and separately an immunohistochemistry technique using a phospho-specific anti-ErbB2 receptor antibody (see Figure 1 and see Figure 6). DiGiovanna fails to teach a method where first the immunoblot technique is used and then the immunhistochemical technique is used for confirmation of the first technique.

However, DiGiovanna teaches that the prior art teaches methods of quantification of tyrosine receptor phosphorylation in tumor samples by immunoprecipitation of receptors and then immunoblotting with an anti-phosphotyrosine antibody, and that such experiments are subject to inaccurate interpretations because of variability in tissue content of stroma/normal cells versus tumor cells and because of tumor cell heterogeneity. DiGiovanna further teaches that use of specific antibody against phospho-Her2 allows direct staining of intact tissue for specific activated receptors (see page 1950, 2nd column). Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have used DiGiovanna's immunohistochemical method to confirm earlier results obtained by immunoprecipitation followed by immunoblotting. One would have been motivated to have done so because of DiGiovanna's teachings that immunoblotting techniques may result in inaccurate interpretations.

New Grounds of Rejection:

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 23-28, 40-52 and 64-73 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The basis of this rejection is that the specification lacks a written description of determining "a significant level of phosphorylation".

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is for purposes of the 'written description' inquiry, "*whatever is now claimed" (*see page 1117). In the present case, the specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is now claimed." (See Vas-Cath at page 1116.)

Claims 23, 47 and 71 have been amended to include the phrase "if a significant level of phosphorylation is determined", so that now the claims include the intended use of using detection of a "significant level" of phosphorylation of an ErbB receptor as way to determine if sample of tumor cells or a patient having a tumor will respond to an antibody inhibiting the association of Her2 with another member of the ErbB receptor family, or in the case of claims 71-73, will respond to any anti-Her2 antibody. However, the specification fails to provide a description of the levels of phosphorylation of an ErbB receptor that are significant for the purposes of the method. The only teaching relating to any level of phosphorylation is in

Example 5, where the word "strong" is used to describe the level of phosphorylation of Her2 in examples of responsive tumors. However, this does not provide written description for the concept of "significant level of phosphorylation", because the word "significant" may encompass a level that is less than "strong", but large enough to lead one to decide that a tumor or tumor cell might be responsive to therapy. However, the specification contains no discussion concerning what is meant by the concept of a significant level of phosphorylation, and the meaning of "significant level" cannot be discerned from the working examples. In Figure 4, the presence of Her2 phosphorylation in unresponsive tumors is noted by the examiner, but it is not clear from the data presented how the levels of phosphorylation in the unresponsive tumors differ from that of the responsive tumors, because the variability of Her2 phosphorylation in the responsive tumors appears to be high.

10. Claims 23-28, 40, 42-44, 47-52, 64, 66, and 70 are rejected under 35 U.S.C. 102(b) as being anticipated by DiGiovanna (DiGiovanna, M.P. et al. Cancer Research 55: 1946-1955, 1995; of record).

DiGiovanna teaches methods of detecting levels of ErbB2 phosphorylation in samples of SKBr3 cells by immunoblot (see Figure 1). DiGiovanna also teaches methods of detecting levels of ErbB2 phosphoryalation in samples of tumors from patients with overexpressed ErbB2 (see page 1950, 1st to 2nd column). Therefore, DiGiovanna teaches the claimed methods.

The steps of either "identifying said Her2 –positive cells as responsive to treatment" or "predicting that said subject is likely to respond to treatment" are not considered to be active steps. Instead these phrases are considered to be recitations of mental activity. In a method

claim, the presence of steps directed to mental activity does not serve to distinguish that claimed method over a prior art method containing active steps identical to active steps in the claimed method.

The intended use of the claimed methods is for identifying tumor cells as responsive to treatment with an antibody inhibiting the association of HER2 with another member of the ErbB receptor family, wherein the antibody binds HER2, or the anti-Her2 antibody blocks ligand activation of an ErbB heterodimer comprising HER2 or wherein the antibody is rhuMAb 2C4. The intended use may also be for predicting the response of a subject diagnosed with a HER2-positive tumor to treatment with an antibody inhibiting the association of HER2 with another member of the ErbB receptor family. DiGiovanna's method may have the same intended use as the intended uses of the claimed methods with respect to the broad claims of predicting efficacy of a treatment directed to inhibiting signaling by Her2. Whether or not DiGiovanna has failed to establish the efficacy of using methods of detecting Her2 phosphorylation for the purpose of predicting responsiveness to an anti-Her2 antibody that inhibits the association of Her2 with another member of the ErbB receptor family does not appear to be the relevant issue when comparing the claimed methods with DiGiovanna's methods, because there is no evidence of record demonstrating a reason related to the active steps of the claimed methods why DiGiovanna's methods could not have been used for the intended uses of the claimed methods. For example, it is noted that the working examples of the present application use the same antibody as does DiGiovanna for the detection of Her2 phosphorylation. The active steps in DiGiovanna are the same as in the claims and the intended use recited in the claims does not appear to materially affect the active steps of the claimed methods.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne Holleran, whose telephone number is (571) 272-0833. The examiner can normally be reached on Monday through Friday from 9:30 am to 5:00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms, can be reached on (571) 272-0832. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Papers related to this application may be submitted to Group 1600 by facsimile transmission. The faxing of such papers must conform to the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The Official Fax number for Group 1600 is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll free).

Anne L. Holleran
Patent Examiner
March 2, 2007

LARRY R. HELMS, PH.D.
SUPERVISORY PATENT EXAMINER